DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

TO: All Institutions Conducting Human Gene Transfer Research

FROM: Amy P. Patterson, M.D., Director, Office of Recombinant DNA Activities

SUBJECT: Requirements for Reporting Serious Adverse Events: Request for Institutional Review

The *NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines)* require the immediate reporting of serious adverse events associated with human gene transfer clinical research. The purpose of this memorandum is to request that you conduct a review to ensure that your institution is in compliance with these requirements.

The *NIH Guidelines* apply to all NIH-funded projects involving recombinant DNA techniques as well as to all non-NIH funded research involving recombinant DNA techniques conducted at or sponsored by an institution that receives NIH funds for projects involving such techniques. The requirements for reporting serious adverse events in human gene transfer research are found at Appendix M-VII-C in the *NIH Guidelines*. Appendix M-VII-C states:

> Investigators who have received approval from FDA to initiate a human gene transfer protocol must report any serious adverse event immediately to the local Institutional Review Board, Institutional Biosafety Committee, Office for Protection from Research Risks (if applicable), NIH/ORDA, and FDA, followed by the submission of a written report filed with each group. Reports submitted to NIH/ORDA shall be sent to the Office of Recombinant DNA Activities, National Institutes of Health/MSC 7010, 6000 Executive boulevard, Suite 302, Bethesda, Maryland 20892-7010, 301-496-9838.

As stated in Section I-D of the *NIH Guidelines*, noncompliance may result in: (i) suspension, limitation, or termination of NIH funds for recombinant DNA research at the institution, or (ii) a requirement for prior NIH approval of any or all recombinant DNA projects at the institution.

Please review all ongoing gene transfer clinical trials being conducted at your institution for compliance with the reporting requirements as specified in Appendix M-VII-C. Note that all serious adverse events should be reported regardless of whether or not they are thought to be related to the gene transfer intervention. If, in the course of this review, you find that serious adverse events have not been reported as required, please submit the requisite reports to the NIH Office of Recombinant DNA Activities (ORDA). The Serious Adverse Event Reporting Form found on the NIH/ORDA web site (http://www.nih.gov/od/orda/) should be used for this purpose and for reporting any future serious adverse events.

The *NIH Guidelines* (Section IV-B) require that your institution have policies and procedures to ensure compliance with the *NIH Guidelines*. As part of this review, please send to ORDA a description of your specific policies and procedures which relate to the serious adverse event reporting requirements in the *NIH Guidelines*.

NIH recently published *a Federal Register* notice outlining proposed changes to the *NIH Guidelines* regarding the reporting and public disclosure of serious adverse events. A copy of the notice can be found on the NIH/ORDA web site (http://www.nih.gov/od/orda/). The proposed changes add a definition of serious adverse event; stipulate the time-frame in which serious adverse events are to be reported; mandate that serious adverse event reports not contain any trade secret or commercial or financial information that is privileged or confidential; emphasize that all information in the adverse event report is to be considered public; and, in order to protect patient confidentiality, direct that serious adverse event reports be stripped of individually identifiable patient information. At its upcoming meeting on December 8-10, 1999, the NIH Recombinant DNA Advisory Committee will consider public comments and make recommendations regarding the proposed changes.

Please submit all information requested in this memorandum to Director, NIH Office of Recombinant DNA Activities, 6000 Executive Boulevard, Suite 302, Bethesda, Maryland 20892, by December 13, 1999. If you have any questions about this memorandum, please contact Dr. Eugene Rosenthal at 301-496-9838. Thank you for attention to this important matter.

cc:
Principal Investigators
Institutional Biosafety Committees
Members, Recombinant DNA Advisory Committee
Office for Protection from Research Risks
Dr. Harold Varmus, NIH
Dr. Ruth Kirschstein, NIH
Dr. Lana Skirboll, NIH
Dr. Kathryn Zoon, FDA